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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,627	09/21/2006	Reynir Eyjolfsson	2476.0090000/RWE/JSO	1689

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EXAMINER	
SOROUSH, ALI	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
10/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,627	EYJOLFSSON, REYNIR	
	Examiner	Art Unit	
	ALI SOROUSH	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8-11* is/are rejected.

7)☒ Claim(s) *6 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-11 are currently pending examination for patentability.

Double Patenting

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-11 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1 and 3-12 of copending Application No. 11/777849. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claim Objections

Claims 6 and 7 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant recites in the claims "Compactrol" as the calcium sulphate dihydrate. However, Compactrol is simply the trade name for calcium sulphate dihydrate. The claim scope is uncertain since the trade name cannot be used properly to identify any particular material or product. (See MPEP 217305(u)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue; and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-4, 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlan et al. (US Patent Application 2003/0148960 A1, Published 08/7/2003, Filed 10/04/2002) in view of Stofik et al. (US Patent Application 2003/0215526 A1, Published 11/20/2003, Filed 03/07/2003).

Applicant Claims

Applicant claims a tablet formulation comprising 0.5-5.0% w/w of ramipril, 50-90% w/w of calcium sulphate dihydrate, 0.1-5.0% w/w of sodium hydrogen carbonate, and optionally in combination with a disintegrant, binder, lubricant, and other excipients.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

MacLaughlan et al. teach “Combinations of ACE inhibitors and an aldosterone receptor antagonist are described for use in treatment of circulatory disorders." (See abstract). ACE inhibitors are selected from the group consisting of captopril, enalapril, and ramipril. (See claim 4). "Of particular interest are therapies using captopril or enalapril co-administered with low-dose of spironolactone." (See abstract). "A diuretic agent may be used with the combination of ACE inhibitor and aldosterone receptor antagonist. Such diuretic agent may be selected from several known classes, such as thiazides and related sulfonamides, potassium-sparing diuretics, loop diuretics and organic mercurial diuretics. Examples of thiazides are .... hydrochlorothiazide ..." (See paragraphs 0080 and 0081). "For therapeutic purposes, the active components of this combination therapy invention are ordinarily combined with one or more adjuvants appropriate to the indicated route of administration." (See paragraph 0124). "For oral adminsitration, the pharmaceutical composition may be in the form of, for example, a tablet, capsule, suspension or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. Examples of such dosage units are tablets or capsules. The ACE inhibitor may be present in an amount from about 1 to 200 mg, preferably from about 2 to 150

mg, depending upon the specific ACE inhibitor selected. A suitable daily dose for a mammal may very widely depending on the condition of the patient and other factors." (See paragraph 0119). "The dosage regimen for treating a disease condition with the combination therapy of this invention is selected in accordance with a variety of factors including the type, age, weight, sex and medical condition of the patient, severity of the disease, the route of administration, and the particular compound employed, and thus may vary widely." (See paragraph 0123). In a particular example MacLaughlan et al. teach an oral dosage was prepared and compressed into a tablet comprising 14.3 mg (9.2%) enalapril, 12.5 mg spironolactone, 100 mg (64.2%) calcium sulfate dihydrate, 15 mg sucrose, 8 mg (5.1%)starch, 4 mg (2.6%) talc, and 2 mg stearic acid. (See paragraph 0129).

Stofik et al. teach, “Disclosed is pharmaceutical compositions comprising: a) a therapeutically effective amount of an ACE inhibitor which is susceptible to degradation or its salt; b) a greater than stoichiometric amount of an alkali or alkaline earth metal carbonate, relative to the amount of ACE inhibitor or its salt; and c) a pharmaceutically acceptable carrier. The degradation may be internal cyclization (DKP formation). The pharmaceutical composition, thus, is characterized by improved stability relative compositions having stiochiometric amounts of the carbonate or less, wherein the improved stability is based on decreased DKP formation." (See paragraphs 0020-0024). “The ACE inhibitors may be selected from groups consisting of … Enalapril … Ramipril …” (See paragraph 0026). “Preferably, the carbonate is sodium bicarbonate." (See paragraph 0025). "The pharmaceutical compositions may further comprise a

disintegrant, a binder, and a lubricant. The pharmaceutically acceptable carrier may be selected from any organic or inorganic substance which is conventionally used in pharmaceutical manufacture, such as filler, a solvent, or a suspending agent. In the pharmaceutical composition, the pharmaceutically acceptable carrier may be a filler selected from the group consisting of … starch, pregelatinized starch …" (See paragraphs 0028 and 0029). "[T]he binder may be selected from Pregelatinized Starch NF … starch …" (See paragraph 0031). "[T]he lubricant may be selected from the groups consisting of … sodium stearyl fumarate … talc …" (See paragraph 0032).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

MacLaughlan et al. teach a composition that comprises calcium sulfate dihydrate, ramirpil, hydrochlorothiazide, starch (disintegrant/binder), and talc (lubricant). MacLaughlan et al. lacks a teaching of a composition comprising sodium hydrogen carbonate (sodium bicarbonate) and further wherein the disintegrant/binder is pregelatinised starch and the lubricant is sodium stearyl fumarate. These deficiencies are cured by Stofik et al.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace enalapril with ramipril in the composition taught by MacLaughlan et al., as suggested by Maclaughlan et al., and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because

MacLaughlan et al. teach that enalapril and ramipril are suitable alternative ACE inhibitors which can be used interchangeably.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add sodium bicarbonate (sodium hydrogen carbonate) to the composition taught by MacLaughlan et al., as suggested by Stofik et al., and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because Stofik et al. teach that with the addition of greater than stoichiometric amount of sodium bicarbonate to the composition taught by MacLaughlan et al. would result in improved stability of the ACE inhibitor by decreasing the formation of DKP.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace starch with pregelatinized starch in the composition taught by MacLaughlan et al., as suggested by Stofik et al., and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because Stofik et al. teach that starch is both a filler and binder and that pregelatinized starch is a suitable alternative for use as a filler and/or binder. With regard to the instant claim that pregelatinized starch is a disintergrant, this claim limitation is an intended use and not given patentable weight in a composition claim.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace talc with sodium stearyl fumurate in the composition taught by MacLaughlan et al., as suggested by Stofik et al., and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because Stofik et al. teach that talc and sodium stearyl fumurate are suitable

alternative lubricants which can be used interchangeably in pharmaceutical formulations.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to adjust the concentrations of the constituent components of the formulation taught by the combined teachings of MacLaughlan et al. and Stofik et al. through routine optimization, as suggested by MacLaughlan et al. and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because MacLaughlan et al. teach that the dosage regimen for treating a disease condition with the combination therapy of this invention is selected in accordance with a variety of factors including age, weight, sex, etc. and thus may very widely.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

2. Claims 1-3, 5, 8, 9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLaughlan et al. (US Patent Application 2003/0148960 A1, Published 08/7/2003, Filed 10/04/2002) in view of Stofik et al. (US Patent Application

2003/0215526 A1, Published 11/20/2003, Filed 03/07/2003) further in view of Chikaraishi et al. (US Patent 6096779, Published 08/01/2000).

Applicant Claims

Applicant claims a tablet formulation comprising 0.5-5.0% w/w of ramipril, 50-90% w/w of calcium sulphate dihydrate, 0.1-5.0% w/w of sodium hydrogen carbonate, and optionally in combination with a disintegrant, binder, lubricant, and other excipients. The formulation further comprises a piretanide.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The combined teachings of MacLaughlan et al. and Stofik et al. is discussed above.

Chikariashi et al. teaches, "Piretanide … is known to be a pharmaceutical agent as a diuretic agent." (See column 1, Lines 10-12).

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

The combined teachings MacLaughlan et al. and Stofik et al. lack a teaching wherein the diuretic is piretanide. This deficiency is cured by Chikariashi et al.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to replace hydrochlothiazide with piretanide in the composition taught by MacLaughlan et al., as suggested by Chikariashi et al., and produce the instant invention. One of ordinary skill in the art would have been motivated to do this because Chikariashi et al. and MacLaughlan et al. teach that both hydrochlorothiazide and piretanide are diuretics and therefore are suitable alternatives for each other.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ali Soroush whose telephone number is (571) 272-9925. The examiner can normally be reached on Monday through Thursday 8:30am to 5:00pm E.S.T.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Mina Haghighatian/
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